

## **REMARKS**

Claims 1-26 and 30-31 are currently pending in the application. By this amendment, the specification and claims 1, 6, 14, 15, 17, 19, 21, 23, 25, 30 and 31 have been amended, and claims 34-38 have been canceled. Claims 27-29 and 32-33 were previously canceled. The foregoing separate sheets marked as "Listing of Claims" shows all the claims in the application, with an indication of the current status of each.

### **Specification**

Examiner has required the cancellation of the reference to incorporation by reference in the paragraph that describes the claim of benefit. Applicant has hereby amended the specification by replacing that paragraph with a replacement paragraph that describes the claim of benefit but does not include a reference to incorporation by reference, thereby addressing Examiner's requirement.

### **Claim Objections: 35 USC § 101**

Examiner has objected to claims 1-26 and 30-31 and 34-38 due to the inclusion of periods, rather than parentheses, within the claims. Further, Examiner has requested clarification of the ending punctuation of claim 26. Claims 1-26 and 30-31 and 34-38 have hereby been amended by replacing the periods within the claim by parentheses, thereby complying with Examiner's and overcoming this portion of the objection. In addition, claim 26 has been amended by deletion of the semicolon (;), which was inadvertently present in the claim before the period, thereby addressing and overcoming Examiner's objection.

In view of the foregoing, Applicant respectfully requests withdrawal of this objection.

### **Claim Rejections: 35 USC § 101**

Claims 1-12, 14-26 and 30-31 stand rejected under 35 USC § 101 as directed to non-statutory subject matter. Applicant notes that claims 34-38 have not been rejected under this statute. Thus, independent claims 1, 6, 14, 30 and 31 have hereby been amended to include the features of dependent claims 34-38, i.e. providing results in the form of a plot or table, and dependent claims 34-38 have hereby been cancelled. Applicant submits that these amendments overcome this rejection, since the subject matter that has been incorporated into the independent claims of the application has been deemed directed to patentable subject matter. Further, these

amendments do not raise any new issues the subject matter of the non-rejected dependent claims having already been considered by the Examiner.

In view of the foregoing, Applicant respectfully requests reconsideration of claims 1-12, 14-26 and 30-31 and withdrawal of this rejection.

**Claim Rejections: 35 USC § 102(b)**

Claims 1-5, 14-22, 34 and 36 stand rejected under 35 USC § 102(b) as anticipated by Gennings et al., (hereafter “Gennings”, *Journal of Agriculture, Biological and Environmental Statistics*, 1998, vol. 3, pages 1-16). This rejection is traversed.

Claims 34 and 36 are hereby canceled, thereby making moot this portion of the rejection.

Applicants have carefully reviewed the Gennings reference and the Examiner’s comments and have found that the Examiner has made numerous technical errors in identifying the elements of the technology described by Gennings and equating those elements with the requirements of the present invention.

Among them, Applicant notes in particular that the Examiner’s analysis of Table 4 (page 8 of Gennings) is incorrect. The Examiner states that Gennings illustrates modeling the interaction of three agents by “removing two of the three agents, and then examining the effects of the mixture on the mixture in Ray 4”, ostensibly equating this to step d of claim 1. However, step d requires: removing at least one subset of agents from the group or mixture, wherein relative ratios of remaining agents (PLURAL) stay the same as in said fixed-ratio ray design. Applicant submits that common sense dictates that the removal of two agents from a group or mixture of three agents does not leave a “group” or “mixture” of agents for further comparison. The concept of retaining the “relative ratios of remaining agents” (required in step d) would be rendered meaningless in such a scenario. In reality, Rays 1-3 of Table 4 depict single chemical data i.e. data obtained with a single agent. Such data is unsuitable and does not fit the requirements recited in step d of claim 1. Further, step e requires: repeating steps b and c for agents remaining in said group or mixture after removal of said subset. Applicant submits that a single chemical (i.e. one chemical) does not constitute a “group” or “mixture” and thus does not fulfill the requirements of claim 1. Applicant offers the following support for the usual understanding

of the words “group” and “mixture” as indicating “more than one”, “at least two”, “two or more”, etc.

In the American Heritage Dictionary (New College Edition) 1980, we read:

Mixture: 2. Anything consisting of diverse elements... 5. (Chemistry) Any composition of two or more substances that are not chemically bound to each other...

Group: 1. As assemblage of persons or objects; 2. Two or more figures that make up a unit or a design... 3. A number of individuals or things considered together because of certain similarities.

In the New Webster's Dictionary (Deluxe Encyclopedic Edition) 1981, we read:

Mixture: ...an assemblage of ingredients mixed together but not chemically combined...any combination of differing elements, kinds or qualities...

Group: Any assemblage of person or things...a number of persons of things arranged or considered together as being related in a scientific, natural or other way...

Pages from the online Merriam Webster dictionary which provide definitions of “group” and “mixture” consistent with those presented above are attached herewith. As can be seen, groups and mixtures require the presence of two or more components. Thus, the Rays of Table 4 cannot serve as the groups or mixtures remaining after a subset of agents is removed.

Further, step e of claim 1 requires the repetition of steps b and c on the agents remaining in the group or mixture after removal of the subset. Gennings neither shows nor suggests such a repetitive analysis.

Claims 1-5 thus clearly are not anticipated by Gennings.

With respect to claim 14, the Examiner states (page 9) “A ‘threshold’ mixture model is used in Gennings because the threshold is used as a cut-off for the departure from additivity in a mixture.” This statement is neither meaningful nor correct. Those skilled in the art recognize that a “threshold” model identifies a join point between doses associated with a background response and doses associated with dose-responsiveness. This is also referred to as a “dose-threshold model”, is illustrated in Figure 2d in Gennings, and is described in the attached article authored by Cox et al., (*Biometrics*, 1987, volume 43, pages 511-523).

In contrast, the present invention as recited in claim 14 is a method for determining an interaction threshold (lines 1 and 6 of claim 14) by using single chemical data and mixture data

below the interaction threshold to predict additivity (line 5 of claim 14), whereas data above the interaction threshold are used to estimate a departure from additivity. The concept and use of an interaction threshold are unique to the present invention and are thoroughly described in the application as filed, for example, in Example 8, particularly in Section 2 which begins at line 27 of page 165. Applicant submits that this concept is neither shown nor suggested by Gennings.

Finally, the Examiner has made several other technical errors in analyzing the Gennings reference, and in equating elements of that reference to the claims of the present invention. Among them, with respect to the rejection of claim 5, confidence intervals comparing the dose threshold for the mixture to that predicted under additivity are *not* the same as the confidence bands on the full dose-response curves as recited in Claim 5.

In view of the foregoing, Applicant respectfully requests reconsideration of claims 1-5 and 14-22 and withdrawal of this rejection.

#### **Claim Rejections: 35 USC § 103(a)**

##### **Gennings**

Claims 6-14, 23-26 and 35 stand rejected under 35 USC § 103(a) as unpatentable over Gennings (as above). This rejection is traversed.

Claim 35 is hereby canceled, thereby making moot this portion of the rejection.

The Examiner's basis for an obviousness rejection based on Gennings is discussed on page 13 of the Office Action. This discussion contains several inaccuracies. Among them, the novelty of the present invention with respect to polynomial terms is not simply the inclusion of higher-order terms in a model, but their interpretation along a fixed-ratio ray. Such an interpretation is neither shown nor suggested by Gennings, who simply presents a response surface on page 1. The response surface on page 1 of Gennings is not at all related to the steps recited in claim 6, where a polynomial model is fit along a fixed ratio ray (step a) and the terms of the model are interpreted, where the number of agents that interact in said group or mixture of agents is equal to the degree of the higher order terms that are not equal to zero (step b).

Further, as discussed above for claim 1, step c of claim 6 requires the removal of at least one subset of agents from the group of mixture of agents with which the data employed in step a is obtained, to form a group or mixture of remaining agents, in which the relative ratios remain

the same. Gennings neither shows nor suggests such a step. In addition, step d of claim 6 requires a repetition of steps a and b, which is also neither shown nor suggested by Gennings. Finally, the analysis of step e, which involves the analysis of the “remaining agents” is also neither shown nor suggested by Gennings.

With respect to claim 14, as discussed above for the 102a rejection, Gennings neither shows nor suggests the concept of interaction thresholds as described in the present application. Thus, Gennings does not render obvious the determination or defining of an interaction threshold as required by lines 1 and 6 of claim 14.

In view of the foregoing, Applicant respectfully requests reconsideration of claims 6-14 and 23-26 and withdrawal of this rejection.

#### **Gennings in view of Schork**

Claims 30-31 and 37-38 stand rejected under 35 USC § 103(a) as obvious over a combination of Gennings (as above) and Schork et al (hereafter “Schork”, US PG PUB 2002/0077775). This rejection is traversed.

Claims 37-38 are hereby canceled, thereby making moot this portion of the rejection.

The lack of applicability of Gennings to the claims of the present application has been discussed above. Schork is cited by the Examiner only to teach the use of computer systems for automation of statistical techniques. As such Schork neither shows or suggests the novel elements of claims 30 and 31. Thus, no combination of Gennings and Schork render the present claims 30-31 obvious.

The inapplicability of the Gennings reference to the methods of the present invention is discussed above under the section dealing with the 102(b) rejection. In that section, Applicant demonstrates that Gennings neither shows nor suggests the subject matter of the present invention.

Examiner cites Schork for the teaching of the use of software in computerized automation of the method. However, Schork deals only with genetic analysis and neither shows nor suggests the prediction of the effects of exposure of a biological system to a combination of many agents. Thus, Schork does not supply the defects of Gennings as a references, and the teachings of Schork, when combined with Gennings, do not render the present invention, as claimed in claims

30 and 31, obvious.

In view of the foregoing, Applicant respectfully requests reconsideration of claims 30-31 and withdrawal of this rejection.

### **Concluding Remarks**

In summary, the sole primary reference applied by the Examiner (Gennings) does NOT anticipate or render obvious the subject matter of the claims in the present application, unique features of which include:

- hypothesis testing and interpretation of subsets of mixtures regarding their impact on the effect of the mixture
- the concept of an interaction threshold
- interpretation of polynomial terms for models along a specified fixed-ratio ray relative to the parameterization of the underlying response surface (e.g. claim 6)
- use of general nonlinear models (e.g. claim 14)

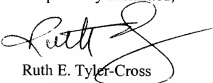
In view of the foregoing, it is requested that the application be reconsidered, that claims 1-26 and 30-31 be allowed, and that the application be passed to issue.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at 703-787-9400 (fax: 703-787-7557; email: ruth@wcc-ip.com) to discuss any other changes deemed necessary in a telephonic or personal interview.

If an extension of time is required for this response to be considered as being timely filed, a conditional petition is hereby made for such extension of time. Please charge any deficiencies in fees and credit any overpayment of fees to Attorney's Deposit Account No. 50-2041.

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Respectfully submitted,



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